

Abstracts

Gregory L. Moneta, MD, Section Editor

Clinical Outcomes of Carotid Endarterectomy in Patients With Carotid Artery Tandem Lesions

Han Y, Park H, Kwon SU, et al. *Stroke* 2014;45:3443-6.



Conclusions: Patients undergoing carotid endarterectomy with the diagnosis of tandem carotid stenosis by contrast-enhanced magnetic resonance angiography have similar rates of stroke and death with and without tandem stenosis.

Summary: There have been previous studies evaluating the outcomes of carotid endarterectomy in patients with both intracranial and extracranial carotid artery disease. Most such studies were published more than 15 years ago using intra-arterial digital subtraction angiography for diagnosis of carotid lesions. The authors sought to reevaluate outcomes of carotid endarterectomy in patients with extracranial and combined intracranial carotid artery stenosis in the modern era where the use of noninvasive diagnostic modalities such as Duplex ultrasonography and contrast-enhanced magnetic resonance angiography are primarily used in the planning of carotid endarterectomy. There were 647 consecutive patients who underwent CEA between January 2001 and December 2010. Tandem stenosis, defined as a significant carotid bifurcation stenosis and identifiable stenosis of $\geq 50\%$ of any downstream distal cerebral artery was identified in 92 patients (14.2%) by contrast enhanced magnetic resonance angiography. Patients with and without tandem stenosis were compared in terms of CEA outcomes. Primary end point was the composite of any stroke, myocardial infarction, or death during the periprocedural period or ipsilateral stroke within 4 years after the CEA. The two groups did not differ in terms of estimated 4-year primary endpoint rates (8.7% vs 3.8%; $P = .07$) for ipsilateral stroke-free ($P = .56$), any stroke-free ($P = .89$), or overall survival ($P = .41$).

Comment: The study confirms the frequency with which tandem lesions are observed in patients undergoing CEA (14.2%) and the fact that tandem lesions are not associated with an increased risk of ipsilateral stroke during follow-up after CEA. The only really unique feature of the study is that it is more modern than previous studies and that the diagnosis of intracranial stenosis was made in a different fashion using MRA rather than catheter based contrast angiography.

Global Sodium Consumption and Death From Cardiovascular Causes

Mozaffarian D, Fahimi S, Singh GM, et al. *N Engl J Med* 2014;371:624-34.



Conclusions: There were 1.65 million deaths from cardiovascular causes in 2010 attributable to sodium consumption above a reference level of 2.0 g per day.

Summary: Increased intake of dietary sodium is associated with elevated blood pressure and adverse cardiovascular outcomes (Frieden TR et al, *N Engl J Med* 2011;365:e27). However, global effects of sodium consumption and the effects according to age, sex, and country have not been clearly established. The authors collected data from surveys on sodium intake as determined by urinary excretion and diet in persons from 66 countries (accounting for 74.1% of adults throughout the world). The data was then used to quantify global consumption of sodium according to age, sex, and country. Effects of sodium on blood pressure according to age, race, and the presence or absence of hypertension were calculated from data in a new meta-analysis of 107 randomized interventions, and the effects of blood pressure on cardiovascular mortality, according to age, were calculated from a meta-analysis of cohorts. Cause-specific mortality was then derived from the Global Burden of Disease Study 2010. Using comparative risk assessment an estimate of the cardiovascular effects of current sodium intake as compared with the referenced intake of 2.0 g of sodium per day according to age, sex, and country was determined. In 2010 the estimated mean level of global sodium consumption was 3.95 g per day, and the regional mean levels ranged from 2.18 to 5.51 g per day. Globally, 1.65 million annual deaths from cardiovascular causes (95% uncertainty interval [confidence interval], 1.10 million to 2.22 million) were attributed to sodium intake above the reference level; 61.9% of these deaths occurred in men and 38.1% occurred in women. These deaths accounted for nearly 1 of every 10 deaths from cardiovascular causes (9.5%). Four of every 5 deaths (84.3%) occurred in

low- and middle-income countries and two of every five deaths (40.4%) were premature (before 70 years of age).

Comment: The data indicate that no region and few countries are spared from the adverse effect of increased sodium consumption on cardiovascular death. The data, however, depends upon extrapolating the effects of sodium on blood pressure to cardiovascular risks. Although this is not definitively established, the effect on cardiovascular disease from hypertension and the effects of sodium consumption on hypertension are supported by extensive experimental and demographic evidence. A meta-analysis of 37 trials has shown no significant adverse effects on blood lipid levels, catecholamine levels or renal function from decreased sodium consumption (Aburto NJ et al, *BMJ* 2013;346:f1326). Therefore it appears there is nothing to be lost and potentially much to be gained by decreasing sodium consumption for adults to less than 2 g per day.

Improved Quality of Life After 1 Year With an Invasive Versus a Noninvasive Treatment Strategy in Claudicants: One-Year Results on the Invasive Revascularization or Not in Intermittent Claudication (IRONIC) Trial

Nordanstig J, Taft C, Hensäter M, et al. *Circulation* 2014;130:939-47.



Conclusions: An invasive treatment strategy improves health-related quality of life and intermittent claudication distance after 1 year in patients with stable lifestyle-limiting claudication receiving current medical management.

Summary: Patients with intermittent claudication are at increased risk for cardiovascular events, cerebrovascular events and premature death but are at low risk of limb loss. Many claudicants will respond with increased walking distance with exercise training, thus risk factor modification and medical treatment and exercise training are standard and accepted first-line treatments of patients with intermittent claudication (IC). However exercise training under supervision is not often available for many patients and many others are poorly compliant with supervised exercise. Evidence for the effectiveness of invasive treatment for intermittent claudication is relatively sparse. Most studies evaluating invasive treatment have used selective inclusion criteria enrolling patients on the basis of vascular lesions (ie, in specific vessel segments or lesions of certain length and severity with suitable anatomy for endovascular treatment). A long list of exclusion criteria in such studies has made it difficult to generalize results to the majority of patients with intermittent claudication. Based on all of this the authors sought to perform what they term "a real world" study to test the hypothesis that an invasive (surgical or endovascular) treatment strategy compared with continued medical therapy would improve health-related quality of life in relatively unselected IC patients already receiving best medical treatment and structured (nonsupervised) exercise training advice. Patients with intermittent claudication underwent clinical and ultrasound assessment and those requesting treatment for claudication were then randomly assigned to invasive ($n = 79$) or noninvasive ($n = 79$) treatment groups. The primary endpoint was health-related quality of life after 1 year assessed with the Medical Outcomes Study Short Form 36 version 1 and Vascular Quality of Life Questionnaire. Secondary endpoints included walking distance on a graded treadmill. The Medical Outcomes Short Form 36 version 1 physical components and 2 Medical Outcomes Study Short Form 36 version 1 physical subscales improved significantly more in the invasive vs the noninvasive group ($P < .001$). Vascular Quality of Life Questionnaire score ($P < .01$) and 3 of 5 domain scores improved significantly more in the invasive vs the noninvasive group. Intermittent claudication distance improved more in the invasive (+124 m) vs the noninvasive (+50 m) group ($P = .003$). Change in maximum walking distance was not significantly different between groups.

Comment: There are several innovative elements in this trial's study design, the primary one of which is to use the health-related quality of life as the primary end point. Most claudication trials have used patency of reconstructions, and treadmill walking distance as primary endpoints in evaluation of treatments for claudication. Benefits in health-related quality of life may include many elements and not just leg symptoms. The concept of patient-centered outcomes is becoming increasingly prevalent in clinical trials. To test the unique approach presented in this trial it also will need to be evaluated in additional studies incorporating longer follow-up and

cost effectiveness strategies. Clearly, however, there is still no clearly accepted optimal treatment for intermittent claudication.

Metabolic Syndrome Predicts Restenosis After Carotid Endarterectomy



Williams WT, Assi R, Hall MR, et al. *J Am Coll Surg* 2014;219:771-7.

Conclusions: Metabolic syndrome is an independent predictor for restenosis after carotid endarterectomy (CEA).

Summary: In modern studies, restenosis after endarterectomy for symptomatic severe carotid artery stenosis occurs at a rate of 5% at 3 years (Arquizaan C et al, *Stroke* 2011;42:1015-20). Other studies suggest that at 15 years after CEA rates of stroke associated with restenosis may be as high as 50% (Fluri F et al, *Cerebrovasc Dis* 2008;26:654-8). Obviously restenosis after CEA therefore has the potential to lead to additional interventions and adverse outcomes. Factors predicting restenosis after CEA however, are poorly understood. The purpose of this study was to examine which risk factors are potentially associated with restenosis after CEA. This is a retrospective study that examined the records of all patients who underwent CEA at the Veterans Affairs Connecticut Healthcare System during a 4-year period. Metabolic syndrome was defined as the presence of 3 or more of the following: hypertension as defined by a blood pressure ≥ 130 mmHg; serum triglycerides ≥ 150 mg/dL; high-density lipoprotein ≥ 40 mg/dL; BMI ≥ 25 kg/m²; and fasting blood glucose ≥ 10 mg/dL. Major adverse events were defined as stroke, death or MI. Restenosis was defined as $>50\%$ stenosis on follow-up imaging studies. There were 78 patients who underwent 79 CEAs during the study period. All patients were male and 76% were Caucasian. Mean age was 72.6 years. Mean duration of follow-up was 5.2 years. 67% of patients had metabolic syndrome. Patients with metabolic syndrome were comparable with those without metabolic syndrome in demographics and preoperative comorbidities except for increased hypertension and diabetes, as expected, and in chronic renal insufficiency ($P = .05$). There was no significant difference in long-term survival or freedom from major adverse events between patients with and without metabolic syndrome. However, restenosis was significantly higher in patients with metabolic syndrome ($P = .02$) and occurred 2 years after CEA in patients with metabolic syndrome only, with a large increase in restenosis after 5 years ($P = .018$). In a multivariable analysis metabolic syndrome remained an independent predictor of restenosis ($P = .01$).

Comment: Most studies examining the rate of restenosis following carotid endarterectomy have shorter periods of follow-up than exhibited here. Although in this small study the authors were unable to demonstrate a difference in major adverse events in the patients with metabolic syndrome vs those without metabolic syndrome, an anatomic goal of carotid endarterectomy is to maintain patency of the artery without restenosis. The data does not allow it to be determined whether control of the individual components of the metabolic syndrome around the time of endarterectomy would reduce late restenosis. It appears patients with metabolic syndrome at the time of CEA are at risk for restenosis and thus could constitute a group of patients for whom more frequent and/or long-term surveillance is warranted. In addition such patients may serve as a target for even more intensive medical management of the individual components of their metabolic syndrome at the time of their original operation.

Preventable Readmissions to Surgical Services: Lessons Learned and Targets for Improvement



Dawes AJ, Sacks GD, Russell MM, et al. *J Am Coll Surg* 2014;219:382-9.

Conclusions: A minority of readmissions may potentially be preventable. Policies aimed at penalizing reimbursements based on readmission rates should use clinical data to focus on inappropriate hospitalization as a measure to promote high quality patient care.

Summary: Vascular surgical patients have overall high readmission rates compared to many other types of patients. As a measure of health care quality, hospital readmissions are a prominent focus currently. The Center for Medicare and Medicaid Services (CMS) proposes using readmission rates as a benchmark to improve care, including targeting them as non-reimbursable events. The study here was designed to describe potentially preventable readmissions after surgery and identify targets for improvement. The study focused on patients discharged from a surgical service over 8 consecutive quarters (Q4 2009 to Q3 2011). A working group of attending surgeons defined terms and created classification schemes. Thirty-day readmissions were identified and reviewed by a 2-physician team. Readmissions were then categorized as unpreventable or preventable, and as targets for future quality improvement intervention. Overall readmission rate was 8.3% (315 of 3789 admissions). The most common indication for initial admission was elective surgery. Among admitted patients in the sample, 28% did not undergo an operation during their index admission. Only

21% (55 of 258) of readmissions were likely preventable based on medical record review. Of the preventable readmissions, 38% of patients were discharged within 24 hours and 60 % within 48 hours. Dehydration occurred more frequently among preventable readmissions ($P < .001$). Infection accounted for more than one-third of all readmissions. Preventable readmissions targets for improvement included closer follow-up after discharge (49%), management of the outpatient setting (42%), and avoidance of premature discharge (9%).

Comment: It is very likely that the complexity of medical care will preclude total elimination of readmissions. Many readmissions actually reflect clinically appropriate care delivery and of course some reflect unnecessary or inappropriate care or discretionary events. This paper is a step in the right direction in that indicates that treating all readmissions as unavoidable events is likely not practical or realistic. Efforts should be geared toward distinguishing preventable from unpreventable readmissions to promote the overall goal of delivery of high-quality care.

Intraplaque Hemorrhage, Fibrous Cap Status, and Microembolic Signals in Symptomatic Patients With Mild to Moderate Carotid Artery Stenosis: The Plaque At RISK Study



Truijman MTB, de Rotte AAJ, Aaslid R, et al. *Stroke* 2014;45:3423-6.

Conclusions: In patients with symptomatic mild to moderate carotid artery stenosis, intraplaque hemorrhage (IPH) and the status of the fibrous cap (FC) are not associated with microembolic signals (MES) as determined by transcranial Doppler (TCD). MRI and TCD therefore likely provide different information on plaque vulnerability.

Summary: The primary way of estimating risk of a carotid artery plaque is the degree of stenosis. However, there are other plaque characteristics that may be important as well. Detection of plaques which are prone to rupture, so-called vulnerable plaques, may help to determine the best therapeutic approach to patients with carotid stenosis, especially patients with mild to moderate carotid artery stenosis. In patients with mild to moderate symptomatic carotid artery stenosis increased risk of stroke or recurrent stroke has been associated with IPH and a thin/ruptured FC as evaluated by MRI, and MES detected with TCD. In this study the authors sought to determine whether the presence of MES differs in patients with and without IPH and a thin/ruptured FC, vs patients with only a thin/ruptured FC but without IPH. This is a multicenter, diagnostic cohort study. Patients ($n = 113$) with recent transient ischemic attack (TIA) or minor stroke in the carotid territory and ipsilateral mild to moderate carotid artery plaque were included. IPH and FC status were dichotomously scored. TCD data was analyzed blinded to results of MRI. TCD measurements were feasible in 105/113, with an average recording time of 219 minutes. A total of 26 MESs were detected in 8 of 105 patients. In 44 of 105 plaques IPH was present. In 92 of 105 plaques FC status was assessable and 36 of these had a thin/ruptured FC. There was no significant difference in the prevalence of MES between patients with and without IPH ($P = .46$) or those with thick vs thin/ruptured FC ($P = .48$).

Comment: The study differs from a previous study that correlated a significant relationship between MES occurrence and the presence of a vulnerable plaque on MRI. Patients in that study (Altaf N, et al. *Radiology* 2011; 258:538-545) had high-grade carotid stenosis compared to mild to moderate carotid artery stenosis in the patients in the current study. It maybe, that the microembolic potential of a vulnerable plaque is enhanced by the flow effects induced by high-grade carotid stenosis. One wonders whether the "vulnerable" plaque in isolation in the carotid circulation is really all that important and only becomes important when associated with significant stenosis. Longer term data focusing on clinical outcomes rather than just analysis of MES signals is needed to answer this sort of question.

Long-Term Follow-Up Study of Endarterectomy Versus Angioplasty in Patients With Symptomatic Severe Carotid Stenosis Trial



Mas JL, Arquizaan C, Calvet D, EVA-3S Investigators. *Stroke* 2014;45:2750-6.

Conclusions: The long-term risk-benefit of carotid stenting (CAS) vs endarterectomy (CEA) for symptomatic carotid stenosis favors CEA and the difference is driven by lower risk of procedural stroke after CEA compared to CAS.

Summary: This study presents long-term follow-up of patients included in the endarterectomy vs angioplasty in patients with symptomatic severe carotid artery stenosis (EVA-3S) trial. This is a randomized control trial of CAS vs CEA in 527 patients who had had recently symptomatic severe carotid stenosis. The trial was conducted in 30 centers in France and